Women's Health Care Bibliography
December 2004

1: AJR Am J Roentgenol. 2004 Dec;183(6):1713-9.
MRI guidance of focused ultrasound therapy of uterine fibroids: early results.
Hindley J, Gedroyc WM, Regan L, Stewart E, Tempany C, Hynnen K, Macdanold N, Inbar Y, Itzchak Y, Rabinovici J, Kim K, Geschwind JF, Hesley G, Gostout B, Ehrenstein T, Hengst S, Sklair-Levy M, Shushan A, Jolesz F.

OBJECTIVE: The purpose of this study was to explore our hypothesis that MRI-guided focused ultrasound therapy for the treatment of uterine fibroids will lead to a significant reduction in symptoms and improvement in quality of life. We describe focused ultrasound therapy applications and the method for monitoring the thermal energy deposited in the fibroids, including the MRI parameters required, in a prospective review of 108 treatments. MATERIALS AND METHODS: Patients presenting with symptomatic uterine fibroids who attained a minimal symptom severity score and who would otherwise have been offered a hysterectomy were recruited. Thermal lesions were created within target fibroids using an MRI-guided focused ultrasound therapy system. The developing lesion was monitored using real-time MR thermometry, which was used to assess treatment
outcome in real time to change treatment parameters and achieve the desired outcome. Fibroid volume, fibroid symptoms, and quality-of-life scores were measured before treatment and 6 months after treatment. Adverse events were actively monitored and recorded. RESULTS: In this study, 79.3% of women who had been treated reported a significant improvement in their uterine fibroid symptoms on follow-up health-related quality-of-life questionnaires, which supports our hypothesis. The mean reduction in fibroid volume at 6 months was 13.5%, but nonenhancing volume (mean, 51 cm(3)) remained within the treated fibroid at 6 months. CONCLUSION: This early description of MRI-guided focused ultrasound therapy treatment of fibroids includes follow-up data and shows that, although the volume reduction is moderate, it correlates with treatment volume and the symptomatic response to this treatment is encouraging.
PMID: 15547216 [PubMed - in process]

2: Am Fam Physician. 2004 Nov 15;70(10):1935-44.
Diagnosis and management of multiple sclerosis.
Calabresi PA.

Multiple sclerosis, an idiopathic inflammatory disease of the central nervous system, is characterized pathologically by demyelination and subsequent axonal degeneration. The disease commonly presents in young adults and affects twice as many women as men. Common presenting symptoms include numbness, weakness, visual impairment, loss of balance, dizziness, urinary bladder urgency, fatigue, and depression. The diagnosis of multiple sclerosis should be made by a physician with experience in identifying the disease. Diagnosis should be based on objective evidence of two or more neurologic signs that are localized to the
brain or spinal cord and are disseminated in time and space (i.e., occur in different parts of the central nervous system at least three months apart). Magnetic resonance imaging with gadolinium contrast, especially during or following a first attack, can be helpful in providing evidence of lesions in other parts of the brain and spinal cord. A second magnetic resonance

scan may be useful at least three months after the initial attack to identify new lesions and provide evidence of dissemination over time. It is critical to exclude other diseases that can mimic multiple sclerosis, including vascular disease, spinal cord compression, vitamin B12 deficiency, central nervous system infection (e.g., Lyme disease, syphilis), and other inflammatory conditions (e.g., sarcoidosis, systemic lupus erythematosus, Sjogren's syndrome). Symptom-specific drugs can relieve spasticity, bladder dysfunction, depression, and fatigue. Five disease-modifying treatments for multiple sclerosis have been approved by the U.S. Food and Drug Administration. These treatments are partially effective in reducing exacerbations and may slow progression of disability.
PMID: 15571060 [PubMed - in process]

3: Am J Epidemiol. 2004 Dec 15;160(12):1205-13.
Glucose Tolerance and Risk of Gestational Diabetes Mellitus in Nulliparous Women Who Smoke during Pregnancy.
England LJ, Levine RJ, Qian C, Soule LM, Schisterman EF, Yu KF, Catalano PM.

Gestational diabetes mellitus has been associated with adverse maternal and infant outcomes, including preeclampsia and fetal macrosomia. Although cigarette smoking has been associated with increased insulin resistance, its effect on gestational diabetes mellitus risk is uncertain. The authors evaluated the effects of smoking on glucose tolerance in a cohort of pregnant women who participated in the Calcium for Preeclampsia Prevention trial, a randomized study of nulliparous women conducted in five US medical centers from 1992 to 1995. Results of screening and diagnostic testing for gestational diabetes mellitus were analyzed. For 3,774 of the 4,589 women enrolled, plasma glucose concentration 1 hour after a 50-g oral glucose challenge and complete information on pregnancy outcome were available; for 3,602 of the women, gestational diabetes mellitus status was known. Adjusted mean 1-hour plasma glucose concentration (mg/dl) was elevated in women who smoked at study enrollment (112.6, 95% confidence interval: 110.0, 115.3) compared with women who had never smoked (108.3, 95% confidence interval: 106.7, 109.8; $p < 0.01$). Women who smoked were at increased risk of gestational diabetes mellitus when criteria proposed by the National Diabetes Data Group were used (adjusted odds ratio = 1.9, 95% confidence interval: 1.0, 3.6). These findings support an association between smoking and gestational diabetes mellitus.
PMID: 15583373 [PubMed - in process]

4: Am J Epidemiol. 2004 Dec 1;160(11):1079-86.
Job stress and breast cancer risk: the nurses' health study.
Schernhammer ES, Hankinson SE, Rosner B, Kroenke CH, Willett WC, Colditz GA, Kawachi I.

Workers tend to perceive certain features of their jobs as harmful to health and are alert to associations between job stress and health outcomes, but few observational studies have evaluated the role of job stress in carcinogenesis. The authors prospectively assessed the association between job strain, measured by Karasek and Theorell's job content questionnaire in four categories (low strain, active, passive, and high strain), and breast cancer risk among participants in the Nurses' Health Study. A total of 37,562 US female registered nurses were followed for up to 8 years (1992-2000), and 1,030 cases of invasive breast cancer were ascertained during that period. All participants were still in the workforce at baseline and completed the job content questionnaire. Adjusted for age, reproductive history, and other breast cancer risk factors, the multivariate relative risks of breast cancer, in comparison with women who worked in low-strain jobs, were 0.83 (95% confidence interval (CI): 0.69, 0.99) for women in active jobs, 0.87 (95% CI: 0.73, 1.04) for women in high-strain jobs, and 0.90 (95% CI: 0.76, 1.06) for women in passive jobs. Findings from this study indicate that job stress is not related to any increase in breast cancer risk.
PMID: 15561987 [PubMed - in process]

5: Am J Prev Med. 2004 Dec;27(5):391-396.
Family history as a risk factor for stroke in young women.
Kim H, Friedlander Y, Longstreth WT Jr, Edwards KL, Schwartz SM, Siscovick DS.

BACKGROUND: Family history of stroke (FHS) is associated with risk of stroke in middle-aged to elderly populations. However, few studies have examined this association in younger women or by stroke type. A population-based, case-control study was conducted to examine the association of FHS and risk of stroke in

young women, and to determine whether the association is independent of other stroke risk factors. METHODS: Cases were women aged 18 to 44 years, with first, nonfatal ischemic (n =49) and hemorrhagic (n = 63) strokes in western Washington State in 1991 to 1995. Demographically similar community controls (n = 446) were identified through random-digit telephone dialing. Information on FHS in first-degree relatives (parents and siblings) and other risk factors was obtained through an interview. Person-years (P-Y) at risk of stroke for relatives of each subject were included in polytomous logistic regression models to adjust for family size. The analysis was conducted between 1999 and 2000. RESULTS: After adjustment for age and P-Y, FHS in first-degree relatives was significantly associated with an increased risk of hemorrhagic (odds ratio [OR]=2.6, 95% confidence interval [CI]=1.5-4.3) and ischemic stroke (OR=2.1, 95% CI=1.2-3.9). FHS remained associated with risk of hemorrhagic stroke (OR=2.4, 95% CI=1.4-4.1) and ischemic stroke (OR=1.8, 95%CI=0.9-3.5) after further adjustment for diabetes, hypertension, hypercholesterolemia, body mass index, physical activity, smoking, alcohol, and family history of myocardial infarction. Findings were similar when associations with parental and sibling FHS were examined separately. CONCLUSIONS: Family history of stroke is a risk factor for both hemorrhagic and ischemic strokes among young women.
PMID: 15556739 [PubMed - as supplied by publisher]

6: Am J Public Health. 2004 Dec;94(12):2098-103.
Health care disparities and cervical cancer.
Bradley CJ, Given CW, Roberts C.

OBJECTIVES: We compared cervical cancer incidence, stage at diagnosis, and survival in Medicaid-insured and non-Medicaid-insured populations. METHODS: We stratified the sample by age and used ordered logistic regression to predict stage at diagnosis and used Cox proportional hazards regression to predict survival. RESULTS: Medicaid insured nearly one quarter of women diagnosed with cervical cancer. The likelihood of late-stage disease was greatest for women who enrolled in Medicaid after diagnosis. Women younger than 65 years who enrolled in Medicaid after diagnosis were more likely to die from cervical cancer than were women who were not insured by Medicaid (hazard ratio=2.40, 95% confidence interval=1.49, 3.86). CONCLUSIONS: Our study underscores the importance of cervical cancer screening programs targeted at low-income women.
PMID: 15569960 [PubMed - in process]

7: Ann Oncol. 2004 Dec;15(12):1749-1759.
Toremifene and tamoxifen are equally effective for early-stage breast cancer: first results of International Breast Cancer Study Group Trials 12-93 and 14-93.
[No authors listed]

BACKGROUND: Toremifene is a chlorinated derivative of tamoxifen, developed to improve its risk-benefit profile. The International Breast Cancer Study Group (IBCSG) conducted two complementary randomized trials for peri- and postmenopausal patients with node-positive breast cancer to compare toremifene versus tamoxifen as the endocrine agent and simultaneously investigate a chemotherapy-oriented question. This is the first report of the endocrine comparison after a median follow-up of 5.5 years. PATIENTS AND METHODS: 1035 patients were available for analysis: 75% had estrogen receptor (ER)-positive primary tumors, the median number of involved axillary lymph nodes was three and 81% received prior adjuvant chemotherapy. RESULTS: Toremifene and tamoxifen yielded similar disease-free (DFS) and overall survival (OS): 5-year DFS rates of 72% and 69%, respectively [risk ratio (RR)=0.95; 95% confidence interval (CI)=0.76-1.18]; 5-year OS rates of 85% and 81%, respectively (RR = 1.03; 95% CI = 0.78-1.36). Similar outcomes were observed in the ER-positive cohort. Toxicities were similar in the two treatment groups with very few women (<1%) experiencing severe thromboembolic or cerebrovascular complications. Quality of life results were also similar. Nine patients developed early stage endometrial cancer (toremifene, six; tamoxifen, three). CONCLUSIONS: Toremifene is a valid and safe alternative to tamoxifen in postmenopausal women with endocrine-responsive breast cancer.
PMID: 15550579 [PubMed - as supplied by publisher]

8: Arch Sex Behav. 2004 Dec;33(6):539-48.
Lifetime depression history and sexual function in women at midlife.
Cyranowski JM, Bromberger J, Youk A, Matthews K, Kravitz HM, Powell LH.

We examined the association between lifetime depression history and sexual function in a community-based sample of midlife women. Specifically, 914 women aged 42-52 who were participants in the Study of Women's Health Across the Nation completed a self-report assessment of their sexual behaviors, sexual desire, sexual arousal, and sexual satisfaction over the past 6 months. On the basis of the Structured Clinical Interview for the DSM-IV , participants were categorized into 1 of 3 lifetime major depressive disorder (MDD) history groups:
no MDD history, single episode MDD, and recurrent MDD. In line with previous reports, women with a history of recurrent MDD reported experiencing less frequent sexual arousal, less physical pleasure, and less emotional satisfaction within their current sexual relationships. Although the groups did not differ in their reported frequency of sexual desire or partnered sexual behaviors, lifetime depression history was associated with increased rates of self-stimulation (masturbation). Associations between lifetime depression history and lower levels of physical pleasure within partnered sexual relationships and higher rates of masturbation remained significant following control for current depressive symptoms, study site, marital status, psychotropic medication use, and lifetime history of anxiety or substance abuse/dependence disorder. Future research is needed to characterize the temporal and etiologic relationships among lifetime depressive disorder, current
mood state, and sexual function in women across the lifespan.
PMID: 15483368 [PubMed - in process]

9: Atherosclerosis. 2004 Dec;177(2):383-9.
Association of high serum concentration of the third component of complement (C3) with pre-existing severe coronary artery disease and new vascular events in women.
Szeplaki G, Prohaszka Z, Duba J, Rugonfalvi-Kiss S, Karadi I, Kokai M, Kramer J, Fust G, Kleiber M, Romics L, Varga L.

Atherosclerosis is an inflammatory disease. The complement system plays an important role in the atherosclerotic process. However, lesser data is available on the possible role of C3 as a risk factor for atherosclerosis. Therefore, in a follow up study we determined C3 levels in 266 patients with pre-existing severe coronary artery disease (CAD) and compared their serum C3 concentrations with the cause of the disease. We investigated whether C3 levels predict the major complications of severe CAD during a 5-year long follow up period in patients, who have received an aorto-coronary bypass graft surgery. C3 concentrations were elevated in the patients with severe CAD compared to 182 healthy controls, and women had higher C3 concentrations than men. Pathological C3 levels (C3>/=1.8g/L) were able to predict major complications of atherosclerosis (death by cardiac events, new acute myocardial infarction, stroke, carotid surgery and peripheral arterial disease) that developed during the follow up period only in women (OR: 4.1, 95% C.I. 1.23-13.61, p = 0.0249) independent of other risk factors for atherosclerosis. Our data supports the assumption that high C3 indicates the progression of atherosclerosis as a special marker of chronic inflammation.
PMID: 15530914 [PubMed - in process]

10: Best Pract Res Clin Gastroenterol. 2004 Dec;18(6):1117-23.
The relation between body mass and gastro-oesophageal reflux.
Nilsson M, Lagergren J.

Obesity has, among physicians, since long been considered to cause gastro-oesophageal reflux. The evidence in support of this belief has been scarce, however. During the last few years some population-based studies have addressed this clinically important issue. These studies demonstrated a clear and dose-dependent association between increasing degrees of overweight and gastro-oesophageal reflux. The mechanisms by which obesity causes reflux are unknown, although there is some limited data suggesting that hiatal hernia may be the causal link between obesity and reflux. Moreover, some evidence has been presented showing that obesity is clearly a stronger risk factor among women than among men, and that the relation between overweight and reflux is substantially augmented by postmenopausal hormone therapy. The data so far
available point in the direction of oestrogens, the activity of which is strengthened by increasing body mass, being responsible for this effect. If the results are repeated in future studies, postmenopausal therapy might be avoided among obese females suffering from

severe reflux. Weight-reduction seems to reduce the risk of symptomatic gastro-oesophageal reflux disease, indicating that such strategy might be a useful tool in the treatment of reflux.
PMID: 15561642 [PubMed - in process]

11: BMC Cardiovasc Disord. 2004 Dec 1;4(1):21 [Epub ahead of print]
Progression of coronary calcification in healthy postmenopausal women.
Hsia J, Klouj A, Prasad A, Burt J, Adams-Campbell LL, Howard BV.

BACKGROUND: Coronary artery calcium score incrementally improves coronary risk prediction beyond that provided by conventional risk factors. Limited information is available regarding rates of progression of coronary calcification in women, particularly those with baseline scores above zero. Further, determinants of progression of coronary artery calcification in women are not well understood. This study prospectively evaluated rates and determinants of progression of coronary artery calcium score in a group of healthy postmenopausal women. METHODS: We determined coronary calcium score by computed tomography and recorded demographic, lifestyle and health characteristics of 914 postmenopausal women, a subset of those enrolled in the Women's Health Initiative Observational Study. The 305 women with calcium score >=10 Agatston units at baseline were invited for repeat scan. This analysis includes the 94 women who underwent second scans. RESULTS: Mean age of study participants was 65 +/- 9 years (mean +/- SD), body mass index was 26.1 +/- 6.1 kg/m2, and baseline calcium score was 162 +/- 220 Agatston units. Mean interval between scans was 3.3 +/- 0.7 years. A wide range of changes in coronary calcium score was observed, from -53 to +452 Agatston units/year. Women with lower scores at baseline had smaller annual increases in absolute calcium score. Coronary calcium scores increased 11, 31 and 79 Agatston units/year among women with baseline calcium score in the lowest, middle and highest tertiles. In multivariate analysis, age was not an independent predictor of absolute change in coronary calcium score. Hydroxymethylglutaryl coenzyme A reductase inhibitor (statin) use at baseline was a negative predictor ($p=0.015$), whereas baseline calcium score was a strong, positive predictor ($p<0.0001$) of progression of coronary calcification. CONCLUSION: Among postmenopausal women with coronary calcium score >=10 Agatston units, rates of change of coronary calcium score varied widely. In multivariate analysis, statin use was a negative independent determinant, whereas baseline calcium score was a strong positive predictor of annual change in coronary calcium score.
PMID: 15574196 [PubMed - as supplied by publisher]

12: Br J Surg. 2004 Dec;91(12):1578-81.
Serum levels of soluble E-selectin in women with breast cancer.
Sheen-Chen SM, Eng HL, Huang CC, Chen WJ.

BACKGROUND:: Increasing evidence suggests that E-selectin contributes to tumour growth and metastasis, possibly by increasing angiogenesis and the adhesion of tumour cells to endothelial cells at distant sites. This study aimed to examine the relationship between preoperative levels of circulating soluble E-selectin and breast cancer. METHODS:: Sixty-four consecutive women undergoing surgery for invasive breast cancer were studied prospectively. Venous blood samples were collected before the operation. A control group consisted of 16 patients with a benign breast tumour (eight with fibrocystic disease and eight with fibroadenoma). Serum concentrations of soluble E-selectin were measured by the quantitative sandwich enzyme immunoassay technique and compared with clinicopathological information. RESULTS:: The mean(s.d.) serum level of soluble E-selectin in patients with invasive breast cancer was 73.7(20.9) ng/ml, compared with 36.3(5.6) ng/ml in the control group ($P < 0.001$). Furthermore, the serum levels of soluble E-selectin were significantly higher in women with oestrogen receptor-negative tumours ($P = 0.001$), poorly differentiated tumours ($P < 0.001$), more advanced primary tumour stage ($P < 0.001$), involved lymph nodes ($P < 0.001$), distant metastases ($P < 0.001$) and more advanced tumour node metastasis (TNM) stage ($P < 0.001$). On multivariate analysis, TNM stage ($P < 0.001$) was found to be an independent factor with regard to higher serum levels of soluble E-selectin. CONCLUSION:: Preoperative serum levels of soluble E-selectin might reflect the severity of invasive breast cancer; further evaluation is warranted.
PMID: 15386328 [PubMed - in process]

13: Breast. 2004 Dec;13 Suppl 1:10-8.

Are all aromatase inhibitors the same? A review of the current evidence.
Janicke F.

Third-generation aromatase inhibitors (AIs)-letrozole, anastrozole, and exemestane-are challenging tamoxifen as the standard endocrine therapy for postmenopausal women with hormone receptor-positive breast cancer. AIs suppress estrogen levels by inhibiting aromatase, the enzyme that catalyzes the final step of estrogen biosynthesis. Studies have shown that AIs are highly effective and safe in the treatment of advanced disease, and more recently, AIs have shown promise in the neoadjuvant, adjuvant, and extended adjuvant settings. However, all AIs are not equal. In direct comparisons with anastrozole, letrozole has demonstrated superior estrogen suppression and clinical response in patients with advanced metastatic breast cancer. In addition, letrozole is the only AI to demonstrate consistent superiority over tamoxifen in the neoadjuvant and first-line advanced breast cancer settings. This publication summarizes the available evidence for the efficacy of all 3 agents throughout the breast cancer continuum.
PMID: 15585378 [PubMed - in process]

14: Breast. 2004 Dec;13(6):515-8.
Estrogen and combined estrogen-progestogen therapy in the menopause and breast cancer.
La Vecchia C.

Most of the data on menopausal hormone therapy (HT) and breast cancer risk available up to the mid-1990s were included in a collaborative reanalysis based on over 52,000 women with and 108,000 without breast cancer. HT increased the risk of breast cancer by about 2.3% per year of use. Subsequent studies have confirmed that breast cancer risk is elevated in current and recent (but not past) HT users and that the relative risk (RR) is higher for users of combined estrogen-progestin treatment than for users of estrogen only, and this higher RR is seen with various types of preparations and different routes of administration. With reference to intervention studies, information on combined HT derives from the Women's Health Initiative (WHI). After 7 years of follow-up, 166 breast cancer cases were recorded in the HT group, as against 124 in the placebo group, corresponding to a RR of 1.24. Data from two other, smaller, randomized studies are available. In a combined analysis of the three randomized trials, 205 cases of breast cancer were observed in the treated groups as against 154 in the placebo groups, corresponding to a pooled RR of 1.27. However, in the estrogen-only component of the WHI population, at 8 years of follow-up 94 cases were observed in the estrogen group, opposed to 124 in the placebo group (RR=0.77). The results recorded in the WHI and the Million Women Study do not confirm the suggestion that breast cancers in women using HT have a
more favorable prognosis. HT has also been related to an increased risk of recurrent breast cancer.
PMID: 15563861 [PubMed - in process]

15: Cancer. 2004 Dec 1;101(11):2509-15.
A tool for predicting breast carcinoma mortality in women who do not receive adjuvant therapy.
Kattan MW, Giri D, Panageas KS, Hummer A, Cranor M, Van Zee KJ, Hudis CA, Norton L, Borgen PI, Tan LK.

BACKGROUND: Among the several proposed risk classification schemes for predicting survival in women with breast carcinoma, one of the most commonly used is the Nottingham Prognostic Index (NPI). The goal of the current study was to use a continuous prognostic model (similar to those that have already been demonstrated to possess greater predictive accuracy than risk group-based models in other malignancies) to predict breast carcinoma mortality more accurately compared with the NPI. METHODS: A total of 519 women who had been treated with mastectomy and axillary lymph node dissection at Memorial Sloan-Kettering Cancer Center (New York, NY) between 1976 and 1979 met the following requirements for study inclusion: confirmation of the presence of invasive mammary carcinoma, no receipt of neoadjuvant or adjuvant systemic therapy, no previous history of malignancy, and negative lymph node status as assessed on routine histopathologic examination. Paraffin blocks were available for 368 of the 519 eligible patients. All available axillary lymph node tissue blocks were subjected to enhanced pathologic analysis. The competing-risk method was used to

predict disease-specific death, and the accuracy of the novel prognostic model that emerged from this process was evaluated using the concordance index. Jackknife and 10-fold cross-validation predictions yielded by this new model were compared with predictions yielded by the NPI. RESULTS: Of the 348 women for whom complete data were available, 73 died of disease; the 15-year probability of breast carcinoma-related death was 20%. On the basis of these 348 cases, the authors developed a prognostic model that took patient age, disease multifocality, tumor size, tumor grade, lymphovascular invasion, and enhanced lymph node staining into account, and using competing-risks regression analysis, they found that this new model predicted disease-specific death more accurately compared with the NPI. CONCLUSIONS: The authors have developed a model for predicting breast carcinoma-specific death with improved accuracy. This tool should be useful in counseling patients with regard to their specific need for adjuvant therapy. (c) 2004 American Cancer Society
PMID: 15495180 [PubMed - in process]

16: Cancer Chemother Pharmacol. 2004 Dec;54(6):546-52. Epub 2004 Aug 17.
Docetaxel and high-dose epirubicin as neoadjuvant chemotherapy in locally advanced breast cancer.
Espinosa E, Morales S, Borrega P, Casas A, Madronal C, Machengs I, Illarramendi JA, Lizon J, Moreno JA, Belon J, Janariz J, de la Puente M, Checa T, Mel JR, Gonzalez Baron M.

PURPOSE: Epirubicin and docetaxel are two of the most active drugs against breast carcinoma. As the achievement of a pathological complete response (pCR) is important for survival of patients with locally advanced disease, we used both drugs as neoadjuvant chemotherapy. PATIENTS AND METHODS: Women with locally advanced or inflammatory breast cancer received epirubicin 120 mg/m2 followed by docetaxel 75 mg/m2, both on day 1, every 21 days for four cycles. Lenograstim was administered for 10 days in all cycles. RESULTS: Of 51 patients included, 50 received a total of 188 cycles, with a median of 4 per patient. The median age was 47 years, tumour stage was IIIA in 14 patients and IIIB in 36. Oestrogen receptors were positive in 65% of tumours. There were 10 clinical complete responses (20%) and 29 partial responses (58%). Surgery consisted of mastectomy in 40 patients and tumorectomy in 6. After surgery, 9 pCR were recorded (18%). One patient progressed and died soon after the end of chemotherapy. After a median follow-up of 22 months, the median disease-free survival was 33.7 months. Grade 3/4 neutropenia was observed in 32% of patients, anaemia in 6%, and thrombocytopenia in 4%. Five patients had febrile neutropenia. There were no
toxic deaths or grade 4 nonhaematological toxicities. CONCLUSIONS: Docetaxel plus high-dose epirubicin showed promising activity in patients with locally advanced and inflammatory breast cancer, at the cost of moderate toxicity.
PMID: 15316749 [PubMed - in process]

17: Clin Breast Cancer. 2004 Dec;5(5):371-6.
Docetaxel and Cisplatin as primary chemotherapy for treatment of locally advanced breast cancers.
Lee YJ, Doliny P, Gomez-Fernandez C, Powell J, Reis I, Hurley J.

A phase II trial was designed to evaluate the effectiveness of docetaxel/cisplatin as primary or neoadjuvant chemotherapy of locally advanced breast carcinoma (LABC). Patients with newly diagnosed breast cancers >/= 5 cm in size by palpation were treated with docetaxel/cisplatin, both at 70 mg/m2 intravenously every 21 days for 4 courses. Upon completion of chemotherapy, all patients underwent modified radical mastectomy with axillary nodal dissection Pathologic complete response (pCR) was defined as absence of any invasive carcinoma in the breast. Standard AC (doxorubicin/cyclophosphamide) at 60 mg/m2 and 600 mg/m2, respectively, for 4 cycles was given as adjuvant therapy to maximally eradicate occult distant disease. Between March 1998 and October 2001, 57 women were entered onto this trial, 28 (49%) with inoperable T4 and inflammatory cancers. Pretreatment median tumor size was 9 cm. Thirty-six patients (63%) had estrogen receptor-positive tumors and 10 patients (18%) had tumors with HER2 overexpression. All tumors became operable after neoadjuvant chemotherapy. Pathologic complete response in the breast was achieved in 15
patients (26%) and pCR in the breast and the axilla was achieved in 11 patients (20%). All neoadjuvant chemotherapy courses were administered at full doses without treatment delays caused by toxicity. The most common side effects were hyperglycemia, anemia, and mild neuropathy. The results of this study suggest

that the docetaxel/cisplatin combination can be an effective and well-tolerated induction treatment of LABC, even in very large mostly HER2-nonoverexpressing tumors.
PMID: 15585076 [PubMed - in process]

18: Clin Breast Cancer. 2004 Dec;5(5):341-7.
Neoadjuvant endocrine therapy in primary breast cancer.
Huober J, Krainick-Strobel U, Kurek R, Wallwiener D.

Neoadjuvant chemotherapy has been employed increasingly in operable breast cancer during recent years. Several randomized trials showed that the chances of breast conserving therapy are being enhanced, and that survival was not compromised by primary systemic therapy compared to adjuvant treatment. Apart from the surgical advantages of tumor downstaging and breast conservation, therapy upfront might offer the chance to predict subsequent response of an individual patient to a given agent in the adjuvant setting. Furthermore, by investigating pre- and posttreatment tumor specimens, the neaodjuvant setting might help to evaluate new predictive biological markers, assess biologic effects of new treatments, and gain insight into molecular mechanisms. For postmenopausal patients with receptor-positive disease who cannot tolerate the toxicities of chemotherapy regimens or are not eligible for immediate surgery, endocrine treatment is emerging as an attractive alternative in the neoadjuvant setting. The new third-generation aromatase inhibitors letrozole and anastrozole have been compared to tamoxifen in 3 well-designed randomized neoadjuvant phase III trials (PO24, IMPACT, and PROACT). These studies showed significantly higher response rates for letrozole than for tamoxifen, and comparable ones for anastrozole. Thus, the primary use of an aromatase inhibitor seems a feasible and safe treatment option for postmenopausal women with early-stage breast cancer who do not wish to or are unable to undergo immediate surgery or preoperative chemotherapy. Further neoadjuvant endocrine trials should help us to elucidate the cross-talk between the different signal transduction pathways and their role in endocrine resistance.
PMID: 15585070 [PubMed - in process]

19: Clin Endocrinol (Oxf). 2004 Dec;61(6):738-46.
Adiponectin is independently associated with insulin sensitivity in women with polycystic ovary syndrome.
Spranger J, Mohlig M, Wegewitz U, Ristow M, Pfeiffer AF, Schill T, Schlosser HW, Brabant G, Schofl C.

Summary objective The polycystic ovary syndrome (PCOS) is associated with obesity and insulin resistance predisposing to diabetes mellitus type 2 and atherosclerosis. Adiponectin is a recently discovered adipocytokine with insulin-sensitizing and putative antiatherosclerotic properties. The aim of the study was to elucidate determinants of circulating adiponectin levels and to investigate the potential role of adiponectin in insulin resistance in PCOS women. patients and measurements Plasma adiponectin and parameters of obesity, insulin resistance and hyperandrogenism were measured In 62 women with PCOS and in 35 healthy female controls. results Both in PCOS and controls, adiponectin levels were lower in overweight or obese women than in normal-weight women, without any difference between PCOS and controls after adjustment for body mass index (BMI). In PCOS and in controls there was a significant correlation of adiponectin with BMI ($r = -0.516$, $P < 0.001$), fasting insulin ($r = -0.404$, $P < 0.001$), homeostasis model sensitivity (HOMA %S) ($r = -0.424$, $P < 0.001$) and testosterone ($r = -0.279$, $P < 0.01$), but no correlation with androstenedione ($r = -0.112$, $P = 0.325$), 17-OH-progesterone ($r = -0.031$, $P = 0.784$) or the LH/FSH ratio ($r = -0.033$, $P = 0.753$). Multiple linear regression analysis revealed that BMI and HOMA %S but not testosterone were independently associated with adiponectin plasma levels, explaining 16% (BMI) and 13% (HOMA %S) of the variability of adiponectin, respectively. In PCOS patients insulin sensitivity, as indicated by continuous infusion of glucose with model assessment (CIGMA %S) was significantly correlated with adiponectin ($r = 0.55$; $P < 0.001$), BMI ($r = -0.575$; $P < 0.001$), waist-to-hip ratio (WHR) ($r = -0.48$; $P = 0.001$), body fat mass assessed by dual-energy X-ray-absorptiometry (DEXA) [Dexa-fat (total) ($r = -0.61$; $P < 0.001$) and Dexa-fat (trunk) ($r = -0.59$; $P < 0.001$)] and with testosterone ($r = -0.42$; $P = 0.001$). Multiple linear regression analysis demonstrated that markers of obesity such as BMI, total or truncal fat mass, age and adiponectin were independently associated with CIGMA %S, and that circulating adiponectin accounted for about 18% of the degree of insulin resistance in PCOS. By contrast, testosterone was not a significant factor, suggesting that PCOS per se did not

affect insulin sensitivity independent from obesity, age and adiponectin. Metformin treatment for 6 months in insulin-resistant PCOS women (n = 9) had no effect on plasma adiponectin (P = 0.59) despite significant loss of weight and fat mass and improvement in hyperandrogenaemia. conclusions PCOS per se is not associated with decreased levels of plasma adiponectin. However, circulating adiponectin is independently associated with the degree of insulin resistance in PCOS women and may contribute to the development and/or maintenance of insulin resistance independent from adiposity.
PMID: 15579189 [PubMed - in process]

20: Clin Infect Dis. 2004 Dec 1;39(11):1732-3; author reply 1733-4.
Risk factors for asymptomatic bacteriuria in women with diabetes.
Ribera Montes Mdel C, Perez RP, Barba CP, Beltran DO, Carbonell VP.
Publication Types: Comment/Letter
PMID: 15578383 [PubMed - in process]

21: Clin Rehabil. 2004 Nov;18(7):737-46.
Effects of aerobic and strength exercise on motor fatigue in men and women with multiple sclerosis: a randomized controlled trial.
Surakka J, Romberg A, Ruutiainen J, Aunola S, Virtanen A, Karppi SL, Maentaka K.

OBJECTIVE: To investigate the effects of aerobic and strength exercise on motor fatigue of knee flexor and extensor muscles in subjects with multiple sclerosis (MS). DESIGN: A randomized controlled trial. SETTING: At Masku Neurological Rehabilitation Centre, Masku, and the Social Insurance Institution, Research Department, Turku, Finland. SUBJECTS: Ninety-five MS patients with mild to moderate disability were randomized into exercise group (n =47) and a control group (n =48). INTERVENTION: Participants in the exercise group attended in a supervised exercise period of three weeks, which was followed by a home exercise programme lasting for 23 weeks. Patients in the control group continued with their normal living. OUTCOME MEASURES: Motor fatigue of knee flexor and extensor muscles was measured during a static 30-s maximal sustained muscle contraction. The decline in force (Nm) during the 30 s was recorded, and a fatigue index (FI) was calculated. Subjective fatigue was measured by using the Fatigue Severity Scale (FSS). The Ambulatory Fatigue Index (AFI) was calculated on the basis of a 500-m walking test. Assessment took place at baseline, at the third week (not for the control group) and at the 26th week. All outcome variables were analysed, men and women together, and some interesting contrasts were analysed by gender. RESULTS: Associations were observed with changes in extension FI and Expanded Disability Status Scale (EDSS) score and mean extension torque (Nm), but not with changes in FI and aerobic or strength exercise activity, mean AFI, mean FSS or in mean knee flexion torque. AFI was decreased in all subject groups (p =0.007). Motor fatigue was reduced in knee flexion (p=0.0014) and extension (ns) among female but not in male exercisers after six months of exercise. The exercise activity of women was 25% higher than that of the men. CONCLUSIONS: Six months of exercise reduced motor fatigue in women, but not in men.
PMID: 15573829 [PubMed - in process]

22: Curr Drug Targets Immune Endocr Metabol Disord. 2004 Dec;4(4):327-33.
The impact of body mass index and type 2 diabetes on breast cancer: current therapeutic measures of prevention.
Resta F, Triggiani V, Sabba C, Licchelli B, Ghiyasaldin S, Liso A, Schittulli F, Quaranta M, Paradiso A, Tafaro E, Guastamacchia E.

Epidemiological data have suggested a possible relationship between obesity, diabetes mellitus and cancer risk, particularly breast cancer. We set out to investigate the effect of body mass index and diabetes mellitus on the presence of breast cancer in the Apulian population. We selected 1,663 women affected with primary breast cancer and 4,702 control patients. All patients with breast cancer underwent surgical excision of the tumor and their tumors were histologically confirmed. The prevalence of type 2 diabetes (8%) in the women affected by breast cancer was significantly higher than in the control group (5%) ($p<0.05$). The majority of the diabetic women affected by breast cancer had a BMI value >25, both in premenopause and in postmenopause. With respect to BMI, the non-diabetic patients with breast cancer in postmenopause showed the same pattern as the diabetic ones. Instead, among the women in premenopause a higher percentage (55%) of patients with a BMI <24.9 was found ($p<0.01$). In the Apulian population, the presence of both type 2 diabetes and elevated values of BMI

(that is in a condition of hyperinsulinemia) were found to enhance the frequency of breast cancer.
PMID: 15578984 [PubMed - in process]

23: Curr Pain Headache Rep. 2004 Dec;8(6):452-6.
Myofascial dysfunction in the pelvis.
Jarrell J.

Chronic pelvic pain is a potentially devastating condition that affects many women with severe consequences. A multifaceted condition, chronic pelvic pain enjoys a diverse etiology, a myriad of treatments, and a correspondingly irregular response to therapy. The condition can be associated with severe physical dysfunction in relation to voiding, defecation, and sexual function. Although emphasis has been placed on surgical approaches to therapy, there is increasing interest in alternative therapies, particularly using the principles of the treatment of myofascial dysfunction.
PMID: 15509458 [PubMed - in process]

24: Diabetes Care. 2004 Dec;27(12):2993-2996.
A Prospective Study of Fruit and Vegetable Intake and the Risk of Type 2 Diabetes in Women.
Liu S, Serdula M, Janket SJ, Cook NR, Sesso HD, Willett WC, Manson JE, Buring JE.
PMID: 15562224 [PubMed - as supplied by publisher]

25: Diabetes Care. 2004 Dec;27(12):2898-904.
Gender difference in the impact of type 2 diabetes on coronary heart disease risk.
Juutilainen A, Kortelainen S, Lehto S, Ronnemaa T, Pyorala K, Laakso M.

OBJECTIVE: To explain the stronger effect of type 2 diabetes on the risk of coronary heart disease (CHD) in women compared with men. RESEARCH DESIGN AND METHODS: The study population consisted of 1,296 nondiabetic subjects and 835 type 2 diabetic subjects aged 45-64 years without cardiovascular disease. The end points were CHD death and a major CHD event (CHD death or nonfatal myocardial infarction). The follow-up time was 13 years. RESULTS: Major CHD event rate per 1,000 person-years was 11.6 in nondiabetic men, 1.8 in nondiabetic women, 36.3 in diabetic men, and 31.6 in diabetic women. The diabetes-related hazard ratio for a major CHD event from the Cox model, adjusted for age and area of residence, was 2.9 (95% CI 2.2-3.9) in men and 14.4 (8.4-24.5) in women, and after further adjustment for cardiovascular risk factors, 2.8 (2.0-3.7) and 9.5 (5.5-16.9), respectively. The burden of conventional risk factors in the presence of diabetes was greater in women than in men at baseline. Prospectively, elevated blood pressure, low HDL cholesterol, and high triglycerides contributed to diabetes-related CHD risk more in women than in men. However, after adjusting for conventional risk factors, a substantial proportion of diabetes-related CHD risk remained unexplained in both genders. CONCLUSIONS: The stronger effect of type 2 diabetes on the risk of CHD in women compared with men was in part explained by a heavier risk factor burden and a greater effect of blood pressure and atherogenic dyslipidemia in diabetic women.
PMID: 15562204 [PubMed - in process]

26: Diabetes Care. 2004 Dec;27(12):2856-62.
Depressive symptoms, insulin resistance, and risk of diabetes in women at midlife.
Everson-Rose SA, Meyer PM, Powell LH, Pandey D, Torrens JI, Kravitz HM, Bromberger JT, Matthews KA.

OBJECTIVE: To examine depression and 3-year change in insulin resistance and risk of diabetes and whether associations vary by race. RESEARCH DESIGN AND METHODS: We analyzed data from 2,662 Caucasian, African-American, Hispanic, Japanese-American, and Chinese-American women without a history of diabetes from the Study of Women's Health Across the Nation. We estimated regression coefficients and odds ratios to determine whether depression (Center for Epidemiological Studies Depression Scale score >/=16) predicted increases in homeostasis model assessment of insulin resistance (HOMA-IR) and greater risk of incident diabetes, respectively, over 3 years. RESULTS: Mean baseline HOMA-IR was 1.31 (SD 0.86) and increased 0.05 units per year for all women (P < 0.0001). A total of 97 incident cases of diabetes occurred. Depression was associated with absolute levels of HOMA-IR (P <

0.04) but was unrelated to changes in HOMA-IR; associations did not vary by race. The association between depression and HOMA-IR was eliminated after adjustment for central adiposity (P = 0.85). Depression predicted a 1.66-fold greater risk of diabetes (P < 0.03), which became nonsignificant after adjustment for central adiposity (P = 0.12). We also observed a depression-by-race interaction (P < 0.05) in analyses limited to Caucasians and African Americans, the only groups with enough diabetes cases to reliably test this interaction. Race-stratified models showed that depression predicted 2.56-fold greater risk of diabetes in African Americans only, after risk factor adjustment (P = 0.008). CONCLUSIONS: Depression is associated with higher HOMA-IR values and incident diabetes in middle-aged women. These associations are mediated largely through central adiposity. However, African-American women with depression experience increased risk of diabetes independent of central adiposity and other risk factors.
PMID: 15562197 [PubMed - in process]

27: Headache. 2004 Nov;44(10):1065-1067.
CHRONIC DAILY HEADACHE AND MEDICATION-OVERUSE HEADACHE.
[No authors listed]

Bentsen L, Jensen R. Mirtazapine is effective in the prophylactic treatment of chronic tension-type headache. Neurology. 2004;62:1706-1711. Background: The tricyclic antidepressant amitriptyline is the only drug with prophylactic efficacy for chronic tension-type headache. However, amitriptyline is only moderately effective, with headache reduction of approximately 30%, and treatment is often hampered by side effects. Mirtazapine is a relatively new so-called noradrenergic and specific serotonergic antidepressant, which is more specific and therefore generally better tolerated. Objective: To evaluate the efficacy of mirtazapine. Methods: Twenty-four nondepressed patients with chronic tension-type headache were included in a randomized, double-blind,
placebo-controlled, crossover trial. All patients had tried numerous other treatments. Mirtazapine 15 to 30 mg/day or placebo was each given for 8 weeks separated by a 2-week wash-out period. Results: Twenty-two patients completed the study. The primary efficacy variable, area-under-the-headache curve (AUC; duration x intensity), was lower during treatment with mirtazapine (843) than during treatment with placebo (1275) (P= .01). Mirtazapine also reduced the secondary efficacy variables headache frequency (P= .005), headache duration (P= .03), and headache intensity (P= .03) and was well tolerated. Conclusions: Mirtazapine reduced AUC by 34% more than placebo in difficult-to-treat patients. This finding is clinically relevant and may stimulate the development of prophylactic treatments with increased efficacy and fewer side effects for tension-type headache and other types of chronic pain. Comment: I am happy to see these results on mirtazepine for chronic tension-type headache (CTTH), and I look forward to prescribing it for daily headache, despite its occasion al adverse events of weight gain and somnolence, similar to amitriptyline. It is probably not quite right to state, as the authors did, that "the tricyclic antidepressant amitriptyline is the only drug with prophylactic efficacy for CTTH." For example, here are two randomized controlled studies suggesting efficacy for two very different medications for CTTH: * Saper JR, Silberstein SD, Lake AE III, Winters ME. Double-blind trial of fluoxetine: chronic daily headache and migraine. Headache. 1994;34:497-502. * Saper JR, Lake AE III, Cantrell DT, Winner PK, White JR. Chronic daily headache prophylaxis with tizanidine: a double-blind, placebo-controlled, multicenter outcome study. Headache. 2002;42:470-482.-Stewart J. Tepper Zwart J-A, Hagen K, Svebak S, Stovner LJ, Holmen J. Analgesic overuse among subjects with headache, neck, and low-back pain. Neurology. 2004;62:1540-1544. Objectives: To examine the prevalence of chronic headache (>/=15 days/month) associated with analgesic overuse in relation to age and gender and the association between analgesic overuse and chronic pain (ie, migraine, nonmigrainous headache, neck, and low-back pain). Methods: In the Nord-Trondelag Health Study 1995 to 1997 (HUNT-2), a total of 51 383 subjects responded to headache questions (Head-HUNT), of which 51 050 completed questions related to musculoskeletal symptoms and 49 064 questions regarding the use of analgesics. Results: The prevalence of chronic headache associated with analgesic use daily or almost daily for >/=1 month was 1% (1.3% for women and 0.7% for men) and for analgesic overuse duration of 3 months 0.9% (1.2% for women and 0.6% for men). Chronic headache was more than seven times more likely among those with analgesic overuse (>/=1 month) than those without (odds ratio [OR]= 7.5; 95%CI: 6.6 to 8.5). Upon analysis of the different chronic pain subgroups separately, the association with analgesic overuse was strongest for chronic migraine (OR = 10.3; 95%CI: 8.1 to 13.0), intermediate for chronic nonmigrainous headache

(OR = 6.2; 95%CI: 5.3 to 7.2), and weakest for chronic neck (OR = 2.6, 95%CI: 2.3 to 2.9) and chronic low-back (OR = 3.0; 95%CI: 2.7 to 3.3) pain. The association became stronger with increasing duration of analgesic use for all groups and was most evident among those with headache, especially those with migraine. Conclusions: Chronic headache associated with analgesic overuse is prevalent and especially chronic migraine is more strongly associated with frequent intake of analgesics than other common pain conditions such as chronic neck and chronic low-back pain. Esposito SB, Gherpelli JL. Chronic daily headaches in children and adolescents: a study of clinical characteristics. Cephalalgia. 2004;24(6):476-482. The clinical characteristics of chronic daily headache were studied in 40 children and adolescents, as well as the associated factors responsible for maintenance of the continuous headache pattern. The study of the clinical headache characteristics, showed a female preponderance (75%), mean age of 11 years old at the first consultation, and onset of headache symptomatology at a mean age of 8.5 years old. The average time interval for the evolution of sporadic headache into chronic daily headache was 1.4 years, and psychosocial stressors were present, acutely or chronically, during the period of headache-frequency increase in 47% of the children. Headaches were classified as transformed migraine (65%), mixed pattern (17.5%), and chronic tension-type headache (17.5%). Sixty percent of patients had mothers with migraine. Data regarding common analgesic use showed an average intake of 11.2 days/month. Romero CE, Baron JD, Knox AP, Hinchey JA, Ropper AH. Barbiturate withdrawal following internet purchase of fioricet. Arch Neurol. 2004;61:1111-1112. Background: The Internet enables businesses to advertise their pharmaceutical products and services without medical supervision. The internet also allows for the unsupervised purchase of medications that may have neurologic consequences. Objective: To describe acute withdrawal delirium following the abrupt discontinuation of Fioricet. Patient: The patient was a 37-year-old woman with a history of depression and migraine headaches but not drug abuse. She developed a florid withdrawal delirium following the discontinuation of a drug she purchased online. The medication, which contained butalbital, was self-administered in escalating doses for the treatment of chronic headaches. Daily doses of up to 750 to 1000 mg were reported. Results: The patient was admitted to the hospital for the treatment of unexplained seizures that were followed by several days of an intense withdrawal syndrome. Little improvement was noted after the administration of benzodiazepines and phenothiazine. After parenteral phenobarbital administration, her symptoms resolved. Conclusions: The withdrawal state from barbiturates is similar to that from ethanol. Tolerance can develop with prolonged abuse, leading to escalating drug doses to achieve the desired effect. The suggested management of both types of withdrawal syndromes is similar, but the relative resistance of the behavioral and autonomic features in patients was remarkable. Physicians should be aware of the ease with which medications can be purchased without supervision from the Internet pharmacies. The magnitude of the number of drugs that are made available through this means creates a proclivity to withdrawal states. Comment: There are two take-home lessons here. The first lesson is that abrupt butalbital discontinuation can produce life-threatening barbiturate withdrawal. Drs. Elizabeth Loder and David
Biondi wrote an indispensable guide to safe withdrawal of these patients in 2003 (Loder E, Biondi D. Oral phenobarbital loading: a safe and effective method of withdrawing patients with headache from butalbital compounds. Headache. 2003;43:904-909). The second lesson is that habituating, potentially life-threatening medications are available with ease on the internet, and we must be vigilant about asking our patients if they supplement our prescriptions. Dr. Steve Peroutka has written eloquently on headache information available on the internet (Peroutka S. Analysis of internet sites for headache. Cephalalgia. 2001;21:20-24). Romero et al's article describes sites for obtaining drugs.-Stewart J. Tepper Bigal ME, Rapoport AM, Sheftell FD, Tepper SJ, Lipton RB. Transformed migraine and medication overuse in a tertiary headache centre-clinical characteristics and treatment outcomes. Cephalalgia. 2004;24:483-490. Studies suggest that a substantial proportion of headache sufferers presenting to headache clinics may overuse acute medications. In some cases, overuse may be responsible for the development or maintenance of a chronic daily headache (CDH) syndrome. The objectives of this study are to evaluate patterns of analgesic overuse in patients consulting a headache centre and to compare the outcomes in a group of patients who discontinued medication overuse to those of a group who continued the overuse, in patients with similar age, sex, and psychological profile. We reviewed charts of 456 patients with transformed migraine (TM) and acute medication overuse defined by one of the following criteria: (1) simple analgesic use (>1000 mg ASA/acetaminophen) > 5 days/week; (2) combination analgesics use (caffeine and/or butalbital) > 3 tablets a day for > 3 days a week; (3) opiate use > 1 tablet a day for > 2 days a week; (4) ergotamine tartrate use: 1 mg PO or

0.5 mg PR for > 2 days a week. For triptans, we empirically considered overuse > 1 tablet per day for > 5 days per week. Patients who were able to undergo detoxification and did not overuse medication (based on the above definition) after 1 year of follow-up were considered to have successful detoxification (Group 1). Patients who were not able to discontinue offending agents, or returned to a pattern of medication overuse within 1 year were considered to have unsuccessful detoxification (Group 2). We compared the following outcomes after 1 year of follow-up: number of days
with headache per month; intensity of headache; duration of headache; headache score (frequency x intensity). The majority of patients overused more than one type of medication. Numbers of tablets taken ranged from 1 to 30 each day (mean of 5.2). Forty-eight (10.5%) subjects took more than 10 tablets per day.
Considering patients seen in the last 5 years, we found the following overused substances: butalbital containing combination products, 48%; acetaminophen, 46.2%; opioids, 33.3%; ASA, 32.0%; ergotamine tartrate, 11.8%; sumatriptan, 10.7%; nonsteroidal anti-inflammatory medications other than ASA, 9.8%;
zolmitriptan, 4.6%; rizatriptan, 1.9%; naratriptan, 0.6%. Total of all triptans, 17.8%. Of 456 patients, 318 (69.7%) were successfully detoxified (Group 1) and 138 (30.3%) were not (Group 2). The comparison between groups 1 and 2 after 1 year of follow-up showed a decrease in the frequency of headache of 73.7% in
group 1 and only 17.2% in group 2 (P < .0001). Similarly, the duration of head pain was reduced by 61.2% in group 1 and 14.8% in group 2 (P < .0001). The headache score after 1 year was 18.8 in group 1 and 54 in group 2 (P < .0001). A total of 225 (70.7%) successfully detoxified subjects in Group 1 returned to an
episodic pattern of migraine, compared to 21 (15.3%) in Group 2 (P < .001). More rigorous prescribing guidelines for patients with frequent headaches are urgently needed. Successful detoxification is necessary to ensure improvement in the headache status when treating patients who overuse acute medications. Comment: This study highlights the difficulties faced in trying to obtain outpatient provision for successful detoxification. Isn't it about time the FDA took a fresh look at the risk/benefits for butobarbital combinations, which are still surprisingly available in the United States? Surely this must signal the death knell for these products. The New England Center for Headache have a tremendous database of knowledge on which to base pragmatic prescribing guidelines. I would endorse their concern and commend the approach they have taken.-David S. Millson Torbey MT, Geocadin RG, Razumovsky AY, Rigamonti D, Williams MA. Utility of CSF pressure monitoring to identify idiopathic intracranial hypertension without papilledema in patients with chronic daily
headache. Cephalalgia. 2004;24:495-502. The aim of the present study was to report on the utility of continuous Pcsf monitoring in establishing the diagnosis of idiopathic intracranial hypertension without papilledema (IIHWOP) in chronic daily headache (CDH) patients. We report a series of patients (n =
10) with refractory headaches and suspected IIHWOP referred to us for continuous Pcsf monitoring between 1991 and 2000. Pcsf was measured via a lumbar catheter and analyzed for mean, peak, highest pulse amplitude, and abnormal waveforms. A 1 to 2 day trial of continuous controlled CSF drainage (10 cc/hour) followed Pcsf monitoring. Response to CSF drainage was defined as improvement in headache symptoms. Patients with abnormal waveforms underwent a ventriculoperitoneal (VPS) or lumboperitoneal (LPS) shunt insertion. All patients had normal resting Pcsf (8 +/- 1 mmHg) defined as ICP < 15 mmHg. During sleep, all patients had B-waves and 90% had plateau waves or near plateau waves. All patients underwent either a VPS or LPS procedure. All reported improvement of their headache after surgery. Demonstration of pathological Pcsf patterns by continuous Pcsf monitoring was essential in confirming the diagnosis of IIHWOP, and provided objective evidence to support the decision for shunt surgery. Increased Pcsf was seen mostly during sleep and was intermittent, suggesting that Pcsf elevation may be missed by a single spot-check LP measurement. The similarity between IIHWOP and CDH suggests that continuous Pcsf monitoring in CDH patients may have an important diagnostic role that should be further investigated. Comment: This study confirms that elevated CSF pressure, as measured by continuous CSF pressure monitoring, may be linked to CDH.-Stewart J. Tepper.
PMID: 15546281 [PubMed - as supplied by publisher]

28: Health Care Women Int. 2004 Sep;25(8):702-29.
Psychological functioning in women with fibromyalgia: a grounded theory study.
Wentz KA, Lindberg C, Hallberg LR.

The aim of this study was to elucidate psychological functioning and psychological processes in women with fibromyalgia. Twenty-one females with fibromyalgia (aged 26-72 years) were interviewed in-depth. The interviews were analysed in line with grounded theory. A core concept, "unprotected self," mirroring childhood conditions and adult psychological functioning, was identified. Intense activity or hypomanic helpfulness often was used as self-regulation in adult life. Later an increased exposure to mental load is accompanied by reduction of cognitive functioning and generalised pain. The phase of persistence of fibromyalgia is marked by reduction of cognitive functions, unprotected psychological functioning, and increased mental load as from crisis and somatic symptoms.
PMID: 15371077 [PubMed - indexed for MEDLINE]

29: Int J Obes Relat Metab Disord. 2004 Dec;28(12):1569-74.
Changes in intake of fruits and vegetables in relation to risk of obesity and weight gain among middle-aged women.
He K, Hu FB, Colditz GA, Manson JE, Willett WC, Liu S.

OBJECTIVE: To examine the changes in intake of fruits and vegetables in relation to risk of obesity and weight gain among middle-aged women. DESIGN: Prospective cohort study with 12 y of follow-up conducted in the Nurses' Health Study. SUBJECTS: A total of 74,063 female nurses aged 38-63 y, who were free of cardiovascular disease, cancer, and diabetes at baseline in 1984. MEASUREMENTS: Dietary information was collected using a validated food frequency questionnaire, and body weight and height were self-reported. RESULTS: During the 12-y follow-up, participants tended to gain weight with aging, but those with the largest increase in fruit and vegetable intake had a 24% of lower risk of becoming obese (BMI> or =30 kg/m2) compared with those who had the largest decrease in intake after adjustment for age, physical activity, smoking, total energy intake, and other lifestyle variables (relative risk (RR), 0.76; 95% confidence interval (CI), 0.69-0.86; P for trend <0.0001). For major weight gain (> or =25 kg), women with the largest increase in intake of fruits and vegetables had a 28% lower risk compared to those in the other extreme group (RR, 0.72; 95% CI, 0.55-0.93; P=0.01). Similar results were observed for changes in intake of fruits and vegetables when analyzed separately. CONCLUSIONS: Our findings suggest that increasing intake of fruits and vegetables may reduce long-term risk of obesity and weight gain among middle-aged women.
PMID: 15467774 [PubMed - in process]

30: J Midwifery Womens Health. 2004 Nov-Dec;49(6):529-38.
Pain at midlife.
Rousseau ME, Gottlieb SF.

Although menopause is a normal developmental milestone through which all women pass, the transition has been long associated with chronic pain conditions that may be more accurately viewed as secondary to aging. Clinicians need to understand management of pain problems women may experience. This article examines pain syndromes including headache, back pain, osteoarthritis, pelvic pain, vulvo-vaginal pain, and burning mouth syndrome.
PMID: 15544982 [PubMed - in process]

31: J Neurosci Res. 2004 Dec 1;78(5):603-24.
Neuroimmunoprotective effects of estrogen and derivatives in experimental autoimmune encephalomyelitis: Therapeutic implications for multiple sclerosis.
Offner H.

The extensive literature and the work from our laboratory illustrate the large number of complex processes affected by estrogen that might contribute to the striking ability of 17beta-estradiol (E2) and its derivatives to inhibit clinical and histological signs of experimental autoimmune encephalomyelitis (EAE) in mice. These effects require sustained exposure to relatively low doses of exogenous hormone and offer better protection when initiated prior to induction of EAE. However, oral ethinyl estradiol (EE) and fluasterone, which lacks estrogenic side effects, could partially reverse clinical EAE when given after the onset of disease. The three main areas discussed in this review include E2-mediated inhibition of encephalitogenic T cells, inhibition of cell
migration into central nervous system tissue, and neuroprotective effects that promote axon and myelin survival. E2 effects on EAE were mediated through Esr1 (alpha receptor for E2) but not Esr2 (beta receptor for E2), as were its antiinflammatory and neuroprotective effects. A

novel finding is that E2 up-regulated the expression of Foxp3 and CTLA-4 that contribute to the activity of CD4(+)CD25(+) Treg cells. The protective effects of E2 in EAE suggest its use as therapy for MS, although the risk of cardiovascular disease may complicate treatment in postmenopausal women. This risk could be minimized by using subpregnancy levels of exogenous E2 that produced synergistic effects when used in combination another immunoregulatory therapy. Alternatively, one might envision using EE or fluasterone metabolites alone or in combination therapies
in both male and female MS patients. (c) 2004 Wiley-Liss, Inc.
PMID: 15515048 [PubMed - in process]

32: J Psychosom Res. 2004 Nov;57(5):451-8.
Menstrual cycle influences on pain and emotion in women with fibromyalgia.
Alonso C, Loevinger BL, Muller D, Coe CL.

OBJECTIVE: This study examined the influence of the menstrual cycle on pain and emotion in women with fibromyalgia (FM) as compared with women with rheumatoid arthritis (RA) and to healthy controls. METHODS: One hundred and twenty-five premenopausal women (21-45 years old) participated in this study (57 with FM, 20 with RA, and 48 controls). Pain and emotion assessments were conducted during the follicular and the luteal phases of the menstrual cycle. RESULTS: Women with FM experienced more pain, menstrual symptoms, and negative affect than did women with RA and the controls. All women reported less positive affect during the luteal phase, although this pattern was more pronounced in women with FM and RA
than in controls. CONCLUSION: Although FM pain did not vary across the menstrual cycle, these results point to the importance of considering the lower level and cyclical nature of positive affect when studying women with chronic pain.
PMID: 15581648 [PubMed - in process]

33: J Psychosom Res. 2004 Nov;57(5):417-22.
Work stress and incidence of newly diagnosed fibromyalgia; Prospective cohort study.
Kivimaki M, Leino-Arjas P, Virtanen M, Elovainio M, Keltikangas-Jarvinen L, Puttonen S, Vartia M, Brunner E, Vahtera J.

OBJECTIVES: We examined the prospective association between occupational stress and incidence of newly diagnosed fibromyalgia. METHODS: Cohort study with questionnaire surveys in 1998 and 2000 completed by 4791 hospital employees (4250 women and 541 men). Stress, as indicated by high workload, low decision latitude, and being a victim of workplace bullying, was assessed in the first survey. Incident cases (n=47) were employees reporting physician-diagnosed fibromyalgia in 2000 but not in 1998. Covariates were sex, age, income, obesity, and smoking. RESULTS: After adjustment for covariates, the odds ratio of incident diagnosed fibromyalgia for workplace bullying was 4.1 (95% CI 2.0-9.6). The corresponding odds ratios for high workload and low decision latitude were 2.1 (1.2-3.9) and 2.1 (1.1-4.0), respectively. CONCLUSION: Stress seems to be a contributing factor in the development of fibromyalgia, but further research is needed to examine whether stress perceptions are affected by undiagnosed fibromyalgia.
PMID: 15581643 [PubMed - in process]

34: J Rheumatol. 2004 Oct;31(10):2036-40.
Interrelations between fibromyalgia, thyroid autoantibodies, and depression.
Ribeiro LS, Proietti FA.

OBJECTIVE: To detect and quantify the association between fibromyalgia (FM) and thyroid autoimmunity. METHODS: This cross-sectional study comprised 146 women with FM and 74 case-controls, all 18 years of age or older. FM was diagnosed according to the American College of Rheumatology 1990 classification criteria. The Mini-International Neuropsychiatric Interview (MINI) was applied for the diagnosis of depression, previously considered as an important confounding factor. Thyroid autoimmunity was defined as the occurrence of detectable antithyroid peroxidase antibodies and/or antithyroglobulin antibodies by the immunometric assay. Cases of diffuse connective tissue diseases and thyroid dysfunctions (hypo or hyperthyroidism) were excluded in both groups. RESULTS: Univariate analysis detected an association between FM and thyroid autoimmunity (odds ratio, OR = 3.87, 95%

confidence interval, CI = 1.54-10.13), depression (OR = 3.94, 95% CI = 1.97-7.93), and age (OR = 1.04, 95% CI = 1.01-1.07). In the final logistic regression model, after adjustment for depression and age, the association between FM and thyroid autoimmunity was strengthened (OR = 4.52, 95% CI = 1.86-11.0). CONCLUSION: Our results suggest an association between FM and thyroid autoimmunity.
PMID: 15468372 [PubMed - in process]

35: Maturitas. 2004 Dec 10;49(4):315-20.
Effects of progestins on estrogen-induced increase in C-reactive protein in postmenopausal women.
Rossi R, Bursi F, Veronesi B, Cagnacci A, Modena MG.

Background: C-reactive protein (CRP) represents an independent risk factor for coronary disease and stroke. Because oral estrogens increase CRP levels, with inflammatory and thrombotic consequences, we determined whether the co-administration of a progestin might modify the estrogenic effect on CRP. Methods: In a non-randomized, non-blinded study, we measured C-reactive protein serum concentrations with high-sensitivity technique (hs-CRP) in 163 healthy postmenopausal women divided into groups as follow: 52 not taking hormones (referent group), and 111 taking hormone replacement therapy (HRT) (42 of whom treated with unopposed estrogen, and 69 with an estrogen/progestin combination). Results: Compared with non-users of hormones, median CRP levels were 66% (95% confidence interval: from 44 to 89%) higher and 112% (95% confidence interval: from 89 to 168%) higher among women using a combined estrogen/progestin regimen
and, respectively, among women taking unopposed estrogen [1.54mg/L in the referent group; 2.56mg/L in the estrogen/progestin group ([Formula: see text]), and 3.27mg/L in the unopposed estrogen group ([Formula: see text])]. Furthermore, there was no difference in CRP distributions between women taking different types of progestins. Conclusion: concurrent progestin administration may attenuate estrogen's pro-inflammatory effects, independently on the type of used progestin.
PMID: 15531127 [PubMed - in process]

36: Maturitas. 2004 Dec 10;49(4):292-303.
Self-reported urogenital symptoms in postmenopausal women: Women's Health Initiative.
Pastore LM, Carter RA, Hulka BS, Wells E.

OBJECTIVE:: To examine the prevalence and correlates of self-reported urogenital symptoms (dryness, irritation or itching, discharge, dysuria) among postmenopausal women aged 50-79. Design: A cross-sectional analysis based on n = 98,705 women enrolled in the US-based Women's Health Initiative observational study and clinical trials. Urogenital symptoms, symptom severity (mild, moderate, severe), and all covariates were self-reported through questionnaires at enrollment. Prevalence rates of each urogenital symptom were examined and logistic regression was used to identify potential correlates. Results: Prevalence rates for each symptom were: dryness, 27.0%; irritation or itching, 18.6%; discharge, 11.1%; and dysuria, 5.2%. Four factors were correlated with two or more symptoms: Hispanic ethnicity (adjusted odds ratio (AOR) = 2.1-3.1 versus white women across all symptoms), obesity (AOR = 2.2 severe discharge versus none, AOR = 3.6 severe irritation/itching versus none), treated diabetes (pills or shots) compared to no diabetes (AOR = 2.4 severe dysuria versus none, AOR = 3.2 severe irritation/itching versus none), and vaginal cream HRT/ERT compared to those who never used HRT/ERT (AOR = 4.4 severe dryness versus none, AOR = 4.6 severe irritation/itching versus none). Factors not associated with the symptoms included sexual activity, age, years since menopause, current smoking, marital status, gravidity, and natural versus surgical menopause.
Conclusions: This is the first report to document urogenital symptoms by race/ethnicity among an exclusively postmenopausal population. We found an elevated prevalence of urogenital symptoms among women who are Hispanic, obese, and/or diabetic. Confirmation of our findings in these subgroups, and, if confirmed, analysis on why these populations are at greater risk, are areas for future research.
PMID: 15531125 [PubMed - in process]

37: Menopause. 2004 Nov-Dec;11(6):714-25.
Recent advances in women's sexual function and dysfunction.

Basson R.

Current reconceptualization of women's sexual response acknowledges that women have many reasons or incentives for engaging in sex over and beyond sexual desire. Normative changes in their sexuality across the life span, with reproductive events, and with duration of relationship are recognized. Psychophysiological and preliminary functional magnetic resonance imaging data clarify that women's subjective experience of arousal may correlate poorly with signals reflective of genital congestion and also correlate poorly with activation of areas of the brain involved in organizing the reflexive genital vasocongestion. These aspects have been incorporated into new models of sexual response. Definitions of women's sexual dysfunction have recently been revised and expanded in keeping with these concepts. Mental well-being and other psychological and biological factors modulating desire, arousability, and response are areas of active research. Current understanding of the pathophysiology of chronic pain can be applied to the chronic intermittent pain and allodynia of chronic dyspareunia.
PMID: 15543024 [PubMed - in process]

38: Obstet Gynecol. 2004 Dec;104(6):1340-6.
Vaginal apex resection: a treatment option for vaginal apex pain.
Lamvu G, Robinson B, Zolnoun D, Steege JF.

OBJECTIVE: Vaginal apex pain is a subset of chronic pelvic pain commonly treated with surgical excision of the vaginal apex. Our objective was to estimate long-term postoperative pain levels, recovery time, and return to sexual function in women who have undergone vaginal apex repair for chronic vaginal apex pain. METHODS: Since 1995, 45 women have undergone vaginal apex repair at our institution. All were asked to complete a questionnaire describing pain levels, sexual function, daily activities, ability to work, and medical therapy before and after surgical repair of the vaginal apex. Demographic background, previous medical history, and surgical history were abstracted from the medical records. Fisher exact and Wilcoxon rank sum tests were used to determine associations among baseline characteristics and various outcomes. McNemar chi(2) testing was use to compare before and after pain levels. RESULTS: Twenty-seven women constituted the study sample and were available for evaluation before and after vaginal apex repair. Sixty-seven percent of respondents experienced resolution of pelvic pain after vaginal apex repair for a median of 20 months. The number of women experiencing pain with daily activities decreased from 92% before vaginal apex repair to 41% after vaginal apex repair, and 30% reported sexual activity without dyspareunia after vaginal apex repair (P = .004). Sixty-one percent of women returned to work after vaginal apex repair. Most patients required continued medical therapy after vaginal apex repair. CONCLUSION: Vaginal apex repair improves general levels of pelvic pain in some patients diagnosed with vaginal apex pain. Pain relief after vaginal apex repair is temporary, and women are likely to need continued medical therapy. LEVEL OF EVIDENCE: II-2.
PMID: 15572500 [PubMed - in process]

39: Osteoporos Int. 2004 Dec 2; [Epub ahead of print]
Clinical effects of strontium ranelate in women with postmenopausal osteoporosis.
Delmas PD.

Postmenopausal osteoporosis has long-term physical, psychological, and social consequences with a major impact on patients' daily life. Treatment for such a chronic disease needs to be clinically effective and well tolerated, and should ultimately result in a beneficial effect on quality of life. The antifracture efficacy of strontium ranelate, 2 g/day orally, an agent that appears to have dissociation effects on resorption and formation, has been assessed in two large, randomized, double-blind, placebo-controlled clinical studies: the Spinal Osteoporosis Therapeutic Intervention (SOTI) trial and the Treatment Of Peripheral Osteoporosis Study (TROPOS), including more than 6,700 postmenopausal women. Pending the results of TROPOS, a 3-year analysis of SOTI results shows that strontium ranelate significantly reduces new vertebral and clinical
vertebral fracture incidence in postmenopausal osteoporotic women. This significant reduction in the risk of clinical and new vertebral fractures has been demonstrated as early as after 1 year of treatment (RR=0.48, p=0.003; and RR=0.51, p<0.001, respectively) and is maintained over 3 years (RR=0.62, p<0.001; and RR=0.59, p<0.001, respectively). This is

accompanied by decreased back pain and body height loss in the strontium ranelate group compared with the placebo group. As strontium ranelate appears to improve clinical signs and is, furthermore, well tolerated especially in the upper gastrointestinal region, this treatment is expected to result in an improved health-related quality of life (HRQoL). Strontium ranelate thus offers significant clinical benefits in terms of efficacy, tolerability, and ease of administration in the treatment of
postmenopausal women with vertebral osteoporotic fractures.
PMID: 15578158 [PubMed - as supplied by publisher]

40: Pharmacotherapy. 2004 Dec;24(12):1692-713.
Pharmacologic treatment of type 2 diabetic dyslipidemia.
Moon YS, Kashyap ML.

Patients with diabetes mellitus have a higher risk for cardiovascular heart disease (CHD) than does the general population, and once they develop CHD, mortality is higher. Good glycemic control will reduce CHD only modestly in patients with diabetes. Therefore, reduction in all cardiovascular risks such as dyslipidemia, hypertension, and smoking is warranted. The focus of this article is on therapy for dyslipidemia in patients with type 2 diabetes. Patients with the metabolic syndrome (insulin resistance) share similarities with patients
with type 2 diabetes and may have a comparable cardiovascular risk profile. Diabetic patients tend to have higher triglyceride, lower high-density lipoprotein cholesterol (HDL), and similar low-density lipoprotein cholesterol (LDL) levels compared with those levels in nondiabetic patients. However, diabetic patients tend to have a higher concentration of small dense LDL particles, which are associated with higher CHD risk. Current recommendations are for an LDL goal of less than 100 mg/dl (an option of < 70 mg/dl in very high-risk patients), an HDL goal greater than 40 mg/dl for men and greater than 50 mg/dl for women, and a triglyceride goal less than 150 mg/dl. Nonpharmacologic interventions (diet and exercise) are first-line therapies and
are used with pharmacologic therapy when necessary. Lowering LDL levels is the first priority in treating diabetic dyslipidemia. Statins are the first drug choice, followed by resins or ezetimibe, then fenofibrate or niacin. If a single agent is inadequate to achieve lipid goals, combinations of the preceding Drugs may be used. For elevated triglyceride levels, hyperglycemia must be controlled first. If triglyceride or HDL levels remain uncontrolled, pharmacologic agents should be considered. Fibrates are slightly more effective than niacin in lowering triglyceride levels, but niacin increases HDL levels appreciably more than do fibrates. Unlike gemfibrozil, niacin selectively increases subfraction Lp A-I, a cardioprotective HDL. Niacin is distinct in that it has a broad spectrum of beneficial effects on lipids and atherogenic lipoprotein subfraction levels. Niacin produces additive results when used in combination therapy. Recent data suggest that lower dosages and newer formulations of niacin can be used safely in diabetic patients with good glycemic control. Current evidence and guidelines mandate that diabetic dyslipidemia be treated aggressively, and lipid goals can be achieved in most patients with diabetes when all available products are considered and, if necessary, used in combination.
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41: Psychosom Med. 2004 Nov-Dec;66(6):852-60.
The relationship of somatization and depression to experimental pain response in women with temporomandibular disorders.
Sherman JJ, Leresche L, Huggins KH, Mancl LA, Sage JC, Dworkin SF.

OBJECTIVE: Patients with temporomandibular pain disorders (TMD) have greater experimental pain perception when compared with pain-free controls. Common psychological features of TMD include somatization and depression. The impact of depression on experimental pain perception has received considerable attention. However, the role of somatization on experimental pain in a chronic pain population has not been explored. METHODS: Fifty-six women with TMD and 59 pain-free controls underwent three experimental pain procedures, including palpation at fixed amounts of pressure, pressure pain thresholds, and an ischemic pain task. Levels of depression and somatization were assessed using the Research Diagnostic Criteria for TMD. Multiple regression analyses were performed to determine the extent to which depression and somatization were associated with experimental pain response. RESULTS: After controlling for characteristic pain intensity and depression, somatization explained a significant proportion of variance in numbers of masticatory sites rated as painful

(R(2) change = 6.7%, p = .046) with the full model explaining 16.4% of the variance (p = .024). This did not meet an adjusted level of statistical significance (p = .008). After controlling for characteristic pain, only depression added significantly to the model predicting ischemic pain threshold and tolerance. The full models including characteristic pain and depression explained 49% and 20% of the variance in ischemic pain threshold and tolerance, respectively. CONCLUSIONS: These findings suggest that depression and somatization are associated with different measures of experimental pain.
Somatization may be related to more attentional and perceptual measures of clinically relevant pain while depression may be related to more behavioral measures of pain.
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